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>Ehrlichiosis/Babesiosis: Parasitology

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Canine ehrlichiosis is an infectious rickettsial disease of dogs, which is characterized by a reduction in cellular blood elements. Synonyms for the disease include canine rickettsiosis, canine typhus, tropical canine pancytopenia, idiopathic hemorrhagic syndrome, canine hemorrhagic fever, and tracker dog disease. Ehrlichia canis was first recognized in Algeria in 1935, and first reported in the United States in 1963. The disease gained prominence due to devastating losses of military working dogs stationed in Vietnam. Ehrlichiosis has been reported from the tropical and subtropical regions throughout the world. Distribution of the disease is related to the distribution of the vector tick, Rhipicephalus sanguineus, the brown dog tick. Canine ehrlichiosis has been diagnosed in most states within the United States. The disease is encountered most frequently in dogs living in the southern states.

E. canis is a small pleomorphic rickettsial organism, which infects circulating mononuclear cells. Although early reports suggested infection of nonhuman primates, the organism is believed to infect only members of the family Canidae. Morulae, which are intracellular inclusions composed of clusters of organisms, are rarely observed in the early stage of infection. Neutrophilic morula, once thought to be a mild strain of E. canis, is now considered to be a new species of Ehrlichia.

E. canis infections have been reported in dogs with simultaneous infection with Babesia canis and Hepatozoon canis (both protozoa), suggesting simultaneous transmission of organisms from vector ticks. Canine infection probably occurs when salivary secretions from the tick contaminate the attachment site during ingestion of a blood meal. E. canis infection can also be introduced in susceptible dogs by way of blood transfusion. This has been accomplished with blood obtained from dogs chronically infected with E. canis up to 5 years in duration. This fact has obvious implications for canine blood donors in endemic regions. Ticks are thought to represent the primary reservoir for the disease and adult R. sanguineus are capable of transmitting E. canis for at least 155 days following detachment from the host. Ticks can obtain E. canis only if engorgement occurs during the acute phase of the disease in dogs.

Following experimental infection, E. canis causes an acute subclinical, and chronic disease phase. After an

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incubation period of 8 to 20 days, the infected dog enters into the acute phase of ehrlichiosis, which lasts 2 to 4 weeks. During this time, the organism multiplies within circulating mononuclear cells and the mononuclear phagocytic tissues of the liver, spleen, and lymph nodes. This causes lymphadomegaly and lymphoreticular hyperplasia of the liver and spleen. Infected cells are transported via blood to other body organs, especially the lungs, kidney, and meninges. Infected cells adhere to the vascular endothelium, inducing a vasculitis and subendothelial tissue infection. Platelet consumption, sequestration, and destruction appear to contribute to thrombocytopenia in the acute phase. Leukocyte counts are variable during the acute phase. Anemia, possibly related to suppression of erythrocyte production and accelerated erythrocyte destruction develops progressively during the acute phase.

The subclinical phase occurs 6 to 9 weeks postinfection and is characterized by persistence of thrombocytopenia, variable leukopenia, and anemia, in the absence of clinical signs. Dogs with adequate immunocompetence eliminate the parasite and do not develop the chronic phase of the disease.

Dogs, which are unable to mount an effective immune response to the organism, are chronically infected. Hyperglobulinemia, not related to the humoral immune response to E. canis, is typically associated with chronic disease. There appears to be a breed predeliction to the development of depressed cell mediated immunity with experimental studies documenting more severe suppression in German shepherds as compared to beagles. This mechanism is thought to explain the frequent occurrence of severe pancytopenia in German shepherds as compared to other dog breeds. The mechanism responsible for bone marrow suppression in chronic ehrlichiosis is as yet not understood.

Clinical signs during the acute phase of disease will vary from depression, anorexia, and fever to severe loss of stamina, weight loss, ocular and nasal discharges, dyspnea, lymphadenopathy, and edema of the limbs or scrotum. Acute phase clinical signs are transient and usually resolve in 1 to 2 weeks without treatment. Thrombocytopenia and leukopenia generally occur 10 to 20 days following infection. Despite moderate to severe thrombocytopenia, hemorrhages are rarely observed. A variety of central nervous system signs, including hyperesthesia, muscle twitching, and cranial nerve deficits, may occur due to inflammation and bleeding into the meninges. Clinical findings in the acute phase of ehrlichiosis can be identical to canine Rocky Mountain Spotted Fever and canine distemper.

Clinical signs associated with the chronic phase of the

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disease would be characterized as mild to asymptomatic in some dogs, while severe in other dogs. For example, it is not unusual in endemic areas to detect hematologic abnormalities due to chronic E. canis infection in clinical healthy dogs being evaluated for heartworm adulticide therapy. Undetected thrombocytopenia in these patients might potentiate the severity of pulmonary hemorrhage associated with thromboembolism. A combination of bleeding tendencies, pallor due to anemia, severe weight loss debilitation, abdominal tenderness, anterior uveitis, retinal hemorrhages, and neurologic signs consistent with meningoencephalitis typify dogs which are chronically affected. Due to immunosuppression, secondary bacterial infections may be documented. Numerous patterns of hemorrhage may occur in dogs with ehrlichiosis. Epistaxis, once considered a hallmark of the disease, occurs infrequently.

In addition to clinical signs, which may be suggestive of ehrlichiosis, severe laboratory abnormalities can contribute to the index of suspicion for the disease. Hematologic abnormalities including pancytopenia, aplastic anemia, or thrombocytopenia, would be consistent with E. canis infection. Thrombocytopenia is the most consistent hematologic abnormality in both the acute and chronic stages of ehrlichiosis. Pancytopenia is documented in less than 25% of cases in recent retrospective clinical studies. Because E. canis causes defective platelet function, bleeding can be detected in dogs with normal or mildly suppressed platelet counts.

Finding E. canis morula in peripheral blood smears or buffy coat smears is diagnostic; however, morula are found only during the first 2 weeks following infection and generally in very low numbers.

Anemia, if present, will vary significantly in degree of severity among affected dogs. Positive Coombs tests suggest that autoimmune damage, due to circulating erythrocyte antibodies, can contribute to an acute hemolytic crisis in some dogs with ehrlichiosis. In this situation, a regenerative anemia may be encountered; however, a nonregenerative anemia is most frequently documented in chronically infected dogs. Bone marrow examination usually reveals a hypocellular marrow with varying degrees of suppression of the erythroid, myeloid, and megakaryocytic series. Hyperplasia of the bone marrow, especially megakaryocy tic hyperplasia occurs in the acute phase of the disease. Plasmacytosis is a frequently reported finding in the bone marrow.

Serum proteins are abnormal in approximately half of canine ehrlichiosis cases. Hyperglobulinemia is characterized by increased beta and/or gamma globulins. Serum protein electrophoresis may reveal a polyclonal or monoclonal gammopathy. A monoclonal gammopathy in

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association with severe bone marrow plasmocytosis could be easily misdiagnosed as a plasma cell myeloma. Hypoalbuminemia occurs in association with protein-losing nephropathy or a reciprocal decrease in albumin associated with hyperglobulinemia. Less frequently encountered laboratory abnormalities include increased alanine aminotransferase, serum alkaline phosphatase, total bilirubin, azotemia, and proteinuria. E. canis does appear to induce a protein-losing nephropathy most likely related to immune complex glomerulonephritis.

Serologic diagnosis utilizing the indirect fluorescent antibody technique (IFA) is currently recommended for confirming a diagnosis of ehrlichiosis. The IFA test for E. canis is highly sensitive and specific. Serologic cross reaction has not been reported in association with Rickettsia rickettsii, Babesia canis, Ehrlichia platys, or Ehrlichia equi. A positive titer is considered indicative of infection, since animals become seronegative within 3 to 9 months after effective treatment.

Tetracycline (66 mg/kg divided TID) represents the treatment of choice for ehrlichiosis. Oxytetracycline is also effective. Clinical improvement may be observed with penicillin or sulfanomides, but the response is variable. Dramatic clinical improvement generally occurs within 24 to 48 hours after initiation of tetracycline in dogs with acute phase or mild chronic phase disease. Hemorrhage and concurrent infection may contribute to the death of chronically affected dogs, despite the initiation of tetracycline therapy. The duration of treatment of chronically affected dogs with severe pancytopenia or aplastic anemia is controversial. Despite clinical improvement and clearance of infection, bone marrow regeneration may require up to 120 days following treatment. Supportive therapy, including fluids, blood transfusion, vitamins, and anabolic steroids are required in some patients. Long-term tetracycline prophylaxsis (6.6 mg/kg once daily) and repositol oxytetracycline (200 mg IM twice weekly) has been utilized in military working dogs to prevent ehrlichiosis. Tick control is encouraged, but does not provide an effective means to prevent the disease.

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